SCN5A gene

sodium voltage-gated channel alpha subunit 5

Normal Function

The *SCN5A* gene belongs to a family of genes that provide instructions for making sodium channels. These channels open and close at specific times to control the flow of positively charged sodium atoms (sodium ions) into cells. The sodium channels produced from the *SCN5A* gene are abundant in heart (cardiac) muscle and play key roles in these cells' ability to generate and transmit electrical signals. These channels play a major role in signaling the start of each heartbeat, coordinating the contractions of the upper and lower chambers of the heart, and maintaining a normal heart rhythm.

Health Conditions Related to Genetic Changes

Brugada syndrome

More than 300 mutations in the *SCN5A* gene have been identified in people with Brugada syndrome, which is a heart condition characterized by an irregular heart rhythm (arrhythmia). *SCN5A* gene mutations also cause sudden unexpected nocturnal death syndrome (SUNDS), which was originally described in Southeast Asian populations. Researchers have since determined that SUNDS and Brugada syndrome are the same disorder.

Some *SCN5A* gene mutations change single protein building blocks (amino acids) in the SCN5A protein. These mutations alter the structure of ion channels made with the SCN5A protein and disrupt the flow of sodium ions into cardiac muscle cells. Other mutations prevent the *SCN5A* gene from producing any functional ion channels, which also reduces the inward flow of sodium ions. A disruption in ion transport changes the way the heart beats, leading to the arrhythmia often found in Brugada syndrome and SUNDS.

familial dilated cardiomyopathy

progressive familial heart block

A few mutations in the *SCN5A* gene have been found to cause progressive familial heart block. This condition alters the normal beating of the heart and can lead to fainting (syncope) or sudden cardiac arrest and death. The *SCN5A* gene mutations change single protein building blocks (amino acids) in the SCN5A protein. Channels made with this altered protein allow little or no sodium to enter the cell. Cardiac cells with these altered channels have difficulty producing and transmitting electrical

signals that coordinate normal heartbeats. Interruption of this signaling causes heart block. Death of these impaired cardiac cells over time can lead to a buildup of scar tissue (fibrosis), worsening the heart block.

Romano-Ward syndrome

More than 200 mutations in the *SCN5A* gene are known to cause Romano-Ward syndrome, often called long QT syndrome. This condition causes the cardiac muscle to take longer than usual to recharge between beats, which can lead to arrhythmia.

The *SCN5A* gene mutations that cause Romano-Ward syndrome include changes in single amino acids and deletions or insertions of a small number of amino acids in the SCN5A protein. Channels made with these altered SCN5A proteins stay open longer than usual, which allows sodium ions to continue flowing into cardiac muscle cells abnormally. This delay in channel closure alters the transmission of electrical signals in the heart, increasing the risk of an irregular heartbeat that can cause fainting (syncope) or sudden death.

sick sinus syndrome

At least 10 mutations in the *SCN5A* gene have been found to cause another heart condition called sick sinus syndrome. This condition affects the function of the sino-atrial (SA) node, which is an area of specialized cells in the heart that functions as a natural pacemaker. The *SCN5A* gene mutations that cause sick sinus syndrome lead to the production of nonfunctional sodium channels or abnormal channels that cannot transport ions properly. The flow of these ions is essential for creating the electrical impulses that start each heartbeat and spread these signals to other areas of the heart. Mutations reduce the flow of sodium ions, which alters the SA node's ability to create and spread electrical signals. These changes increase the risk of abnormally fast or slow heartbeats, which can cause dizziness, light-headedness, syncope, and related symptoms.

other disorders

Variations in the *SCN5A* gene are associated with several other heart conditions. These include potentially life-threatening forms of arrhythmia called atrial fibrillation and ventricular fibrillation. The genetic variations associated with these conditions alter the flow of sodium ions through the channel, which can lead to abnormal heart rhythms and affect the heart's ability to pump blood.

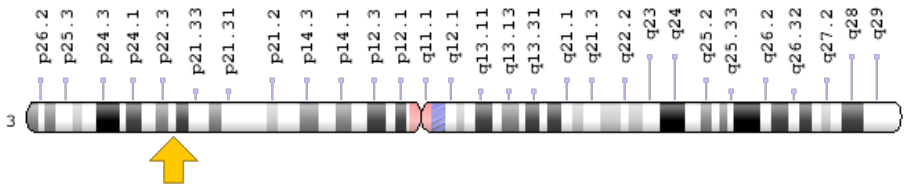
SCN5A gene mutations have also been identified in some cases of sudden infant death syndrome (SIDS). SIDS is a major cause of death in babies younger than 1 year. It is characterized by sudden and unexplained death, usually during sleep. Researchers are working to determine how changes in the *SCN5A* gene could contribute to SIDS. Other genetic and environmental factors, many of which have not been identified, also play a part in determining the risk of this disorder.

Certain drugs, including medications used to treat arrhythmias, infections, seizures, and psychotic disorders, can lead to an abnormal heart rhythm in some people. This drug-induced heart condition, which is known as acquired long QT syndrome, increases the risk of cardiac arrest and sudden death. A small percentage of cases of acquired long QT syndrome occur in people who have an underlying change in the *SCN5A* gene.

Chromosomal Location

Cytogenetic Location: 3p22.2, which is the short (p) arm of chromosome 3 at position 22.2

Molecular Location: base pairs 38,548,061 to 38,649,673 on chromosome 3 (Homo sapiens Annotation Release 108, GRCh38.p7) (NCBI)



Credit: Genome Decoration Page/NCBI

Other Names for This Gene

- HH1
- LQT3
- Nav1.5
- SCN5A_HUMAN
- Sodium channel protein, cardiac muscle alpha-subunit
- sodium channel, voltage gated, type V alpha subunit
- sodium channel, voltage-gated, type V, alpha (long QT syndrome 3)
- sodium channel, voltage-gated, type V, alpha subunit
- SSS1

Additional Information & Resources

GeneReviews

- Brugada Syndrome
  https://www.ncbi.nlm.nih.gov/books/NBK1517
- Dilated Cardiomyopathy Overview
  https://www.ncbi.nlm.nih.gov/books/NBK1309
- Long QT Syndrome
  https://www.ncbi.nlm.nih.gov/books/NBK1129

Scientific Articles on PubMed

- PubMed
  https://www.ncbi.nlm.nih.gov/pubmed?term=%28SCN5A%5BTIAB%5D%29+AND+%28%28Genes%5BMH%5D%29+OR+%28Genetic+Phenomena%5BMH%5D%29%29+AND+english%5Bla%5D+AND+human%5Bmh%5D+AND+%22last+720+days%22%5Bdp%5D

OMIM

- ATRIAL FIBRILLATION, FAMILIAL, 10
  http://omim.org/entry/614022
- CARDIOMYOPATHY, DILATED, 1E
  http://omim.org/entry/601154
- SODIUM CHANNEL, VOLTAGE-GATED, TYPE V, ALPHA SUBUNIT
  http://omim.org/entry/600163
- SUDDEN INFANT DEATH SYNDROME
  http://omim.org/entry/272120
- VENTRICULAR FIBRILLATION, PAROXYSMAL FAMILIAL, 1
  http://omim.org/entry/603829

Research Resources

- Atlas of Genetics and Cytogenetics in Oncology and Haematology
  http://atlasgeneticsoncology.org/Genes/GC_SCN5A.html
- ClinVar
  https://www.ncbi.nlm.nih.gov/clinvar?term=SCN5A%5Bgene%5D
- HGNC Gene Family: Sodium voltage-gated channel alpha subunits
  http://www.genenames.org/cgi-bin/genefamilies/set/1203
- HGNC Gene Symbol Report
  http://www.genenames.org/cgi-bin/gene_symbol_report?q=data/hgnc_data.php&hgnc_id=10593

- NCBI Gene
  https://www.ncbi.nlm.nih.gov/gene/6331
- UniProt
  http://www.uniprot.org/uniprot/Q14524

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